General

Guideline Title

Deep vein thrombosis.

Bibliographic Source(s)

Finnish Medical Society Duodecim. Deep vein thrombosis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2011 Nov 21 [Various].

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Deep vein thrombosis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2010 Aug 3 [Various].

Recommendations

Major Recommendations

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Essentials

- As many as half of all cases of deep vein thrombosis (DVT) develop without clinical symptoms, and only pulmonary embolism (PE) prompts diagnostic tests.
- A normal D-dimer test result is enough to rule out DVT when, based on clinical presentation, the probability of DVT is no more than moderate. However, if the likelihood of DVT is clinically high, diagnostic imaging studies are indicated.
- Before treatment is started, a blood sample should be collected for the analysis of blood clotting factors (thrombophilia screening [see the Finnish Medical Society Duodecim guideline "Inherited thrombophilia"]) if the patient has a positive family history, recurrent or idiopathic (no identified risk factors) thrombosis, massive thrombosis, miscarriage or thrombi affecting both the venous and arterial vessels, or if the patient is young.
- Treatment aims to prevent PE and post-thrombotic syndrome.
- All risk factors, or their absence, must be recorded. They determine the duration of the anticoagulant therapy.

Risk Factors

- DVT is rare if no risk factors are present.
- The most important risk factors for DVT are:

    - Previous venous thrombosis or embolism
    - Severe infection, heart failure
    - Oral contraceptives
    - Oestrogen therapy or pregnancy
    - Immobility (bed rest, flight travel, fractures)
    - Surgery
    - Cancer
    - Inherited thrombophilia (see the Finnish Medical Society Duodecim guideline "Inherited thrombophilia")
- Additional investigations are only performed if they are warranted by the patient history or clinical presentation.
- All risk factors, or their absence, must be recorded. They determine the duration of the anticoagulant therapy (3 months – indefinite).

Clinical Assessment

Clinical Picture

- Common signs and symptoms associated with lower limb DVT are:
    - Oedema (see the Finnish Medical Society Duodecim guideline "Leg oedema"), pain
    - Dilatation of superficial veins
    - Positive Homan's sign (flexion of the ankle causes calf pain)
- As many as half of all cases of DVT develop without clinical symptoms, and only PE prompts diagnostic tests. However, the specificity of the above signs and symptoms is small, particularly when they occur alone (Anand et al., 1998; Goodacre, Sutton, & Sampson, 2005; Wells et al., 2006) [A].
- In addition to the lower limbs, venous thrombosis may also develop occasionally in:
    - An upper limb
    - The pelvic veins
    - Association with a central venous catheter
    - The right heart chambers
    - The portal vein and cerebral venous sinuses

Differential Diagnosis

- Alternate diagnoses to be considered in the differential diagnosis include:
    - Trauma
    - Compartment syndrome
    - Baker's cyst or its rupture
    - Post-thrombotic lower limb oedema

Assessment of Pretest Probability

- The scoring of pretest probability of DVT is presented in Table 1 (below).

Table 1. Assessment of Pretest Probability

Clinical Parameter	Score
Active cancer (treatment ongoing, within 6 months or palliative)	1
Paralysis, paresis or recent plaster immobilisation of a lower limb	1
Recently bedridden for longer than 3 days or major surgery within 4 weeks	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling >3 cm compared with the asymptomatic leg (measured 10 cm below the tibial tuberosity)	1
Pitting oedema (greater in the symptomatic leg)	1
Collateral superficial veins (non-varicose)	1

Clinical Parameter	Score
Alternative diagnosis as likely or greater than that of DVT • 3 points or more = high probability, about 75% risk of DVT • 1–2 points = moderate probability, about 17% risk of DVT • 0 points = low probability, about 3% risk of DVT	2

Wells PS, Anderson DR, Bormanis J et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. Lancet 1997;350:1795-8.

- If the D-dimer test is negative and the score <3, no other investigations are needed.
- If the D-dimer test is positive or the score 3 or higher, compression ultrasonography is indicated.

Investigations

- It is not always necessary to request imaging studies as an emergency procedure, and they can be carried out during normal work hours.
- If there is a high suspicion of venous thrombosis, low molecular weight heparin (LMWH) can be started before the investigations.

D-dimer

- The body's fibrinolytic system is activated in the presence of thrombosis, which results in an increased concentration of D-dimer in the plasma.
- Elevated D-dimer levels are also present in many conditions other than thrombosis (e.g., severe infection/inflammation, cancer, trauma, surgery, pregnancy). Up to 90% of elderly hospitalised patients have elevated D-dimer concentrations as a consequence of infections and tissue damage.
- A normal D-dimer test result is enough to rule out DVT when, based on clinical presentation, the probability of DVT is no more than moderate.
- A normal D-dimer test result together with a negative ultrasonography result does, however, exclude the possibility of DVT with 90%–95% probability.

Ultrasonography

- The investigation is reliable in the diagnosis of proximal DVT (femoral and popliteal veins) but less so in distal DVT.
- In practice, ultrasonography involving only the femoral and popliteal area is sufficient (Bernardi et al., 2008) [A] (2-point ultrasonography, see Videos 1 and 2 in the original guideline document).
- If the ultrasonography result is not consistent with the clinical picture and the D-dimer test is positive, ultrasonography should either be repeated in one week's time or venography is indicated.

Venography

- Venography (a contrast medium examination of the lower limb veins) is indicated if:
  - The ultrasonography result is inconclusive.
  - Laboratory findings are unclear.
  - No other explanation can be found for the symptoms.
- Plasma creatinine must be checked.
- The radiation exposure is minimal and, for example, pregnancy is not a contraindication to the investigation. However, an obstetrician should be consulted before the investigation is carried out.

Other Laboratory Tests

- Before treatment is started, a blood sample should be collected for the analysis of blood clotting factors (thrombophilia screening [see the Finnish Medical Society Duodecim guideline "Inherited thrombophilia"]) if the following apply to the patient (currently or in the past):
  - A positive family history
  - Recurrent or idiopathic (no identified risk factors) thrombosis
  - Massive thrombosis
  - A young patient
  - Miscarriage
  - Thrombi affecting both the venous and arterial vessels

Treatment

- The aim of treatment in lower limb DVT is to prevent:
  - PE (see the Finnish Medical Society Duodecim guideline "Pulmonary embolism")
  - The development of lower limb vein insufficiency.
- The decision on whether DVT can be treated in the primary health care (Othieno, Abu Affan, & Okpo, 2007) [C] depends on the clinical picture and the patient's home situation.
- Most cases are treated primarily at the patient's home.
- Hospital treatment is required for:
  - DVT with severe symptoms
  - Submassive and massive PE

Management in Primary Care

- The treatment of both DVT with only a few symptoms and mild PE can be carried out at a health centre, by a district nurse or self administered by the patient. Based on the individual situation, the treating physician will decide where the treatment should be carried out.
  - Obese patients will need two daily injections because of the large doses needed.
  - Patients with several comorbidities or renal failure are usually not suitable for home treatment.
  - The patient must be supplied with written instructions on how to carry out the treatment.
- If treatment is carried out at home, the following must be ensured:
  - Correct injection technique and correct dose
  - Adequate monitoring of the anticoagulant therapy
  - Instructions regarding compression bandages and stockings
  - Monitoring the patient for possible complications (bleeding, emboli)
- A follow-up appointment should be made at the latest when the anticoagulant therapy is about to finish.
  - The patient is asked about his/her health and checked for signs of recurrence and post-thrombotic syndrome.

Anticoagulant Therapy: Dose and Duration

- LMWH is principally used to treat:
  - DVT below the knee and at the thigh level
  - More proximal thrombi provided no severe symptoms are present
- Dalteparin by subcutaneous injection 100 units/kg twice daily or 200 units/kg once daily.
- Enoxaparin by subcutaneous injection 1 mg/kg twice daily or 1.5 mg/kg once daily.
- Warfarin is started concomitantly, either 5 mg/day or with the estimated maintenance dose for 3 days and then as guided by international normalised ratio (INR) readings.
- Heparin is continued:
  - Until INR has been within the target range (2.0–3.0) for 2 days
  - In any case for at least 5 days
- Fondaparinux is an alternative for LMWH. It is suitable for patients with heparin allergy and for the treatment of heparin-induced thrombocytopenia (HIT).
- LMWH is suitable during pregnancy. Breast feeding is not a contraindication to warfarin.
- Patients treated for active cancer can be managed with LMWH for 3–6 months followed by warfarin.
- Duration of anticoagulant therapy, see Table 2.

Table 2. Duration of Anticoagulant Therapy

Indications	Duration
First episode of thrombosis with a transient risk factor present (e.g., surgery, trauma, immobility, hormonal contraception or replacement therapy, pregnancy)	3–6 months
First episode of unprovoked thrombosis	At least 6 months
First episode of thrombosis in a patient with: • Cancer	Indefinite

Indications	Duration
• Anticardiolipin antibodies or lupus anticoagulant in repeated tests (with a 3 month interval) • Homozygous factor V or prothrombin (factor II) gene mutation • Established antithrombin deficiency • Established protein C or S deficiency • Combination of two or more thrombophilias	
Recurrent unprovoked thrombosis	Indefinite

Thrombolytic Therapy (Fibrinolytic Therapy)

- Thrombolysis (Watson & Armon, 2004) [B] may be attempted if the thrombus
  - Is recent (less than 1 week) and
  - Extends above the inguinal ligament or proximally in an upper limb thrombosis and
  - Causes severe symptoms and significant oedema.
- Thrombolysis can be considered if all the above criteria are fulfilled and the patient is not at an increased risk of bleeding.
- Local, catheter-directed thrombolysis is the treatment of choice if a radiologist competent in the procedure is available.

Surgical Treatment

- Surgery is the first-line treatment approach if the viability of the limb is threatened and particularly if both thrombolytic and anticoagulant therapy are contraindicated.

Other Treatment

- Immediate bandaging during the acute phase to ensure the competence of the communicating veins
  - Using an elastic bandage, the leg is bandaged from the foot to the knee gradually decreasing the pressure as the dressing advances proximally.
  - The bandage is applied in circular turns; a figure of eight bandage is too tight.
  - Catheter-directed thrombolysis is not a contraindication to bandaging.
  - If the swelling extends to the thigh, the leg should be bandaged up to the groin.
- The patient should mobilise as soon as clinically possible.
- Follow-up treatment with graduated compression stockings (Class II) for at least 2 years reduces the likelihood of post-thrombotic syndrome (Kolbach et al., 2003) [A].
- Patient education

Related Resources

Refer to the original guideline document for related evidence, including Cochrane reviews, other evidence summaries, clinical guidelines, and literature.

Definitions:

Classification of the Quality of Evidence

Code	Quality of Evidence	Definition
A	High	Further research is very unlikely to change confidence in the estimate of effect. • Several high-quality studies with consistent results • In special cases: one large, high-quality multi-centre trial
B	Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate. • One high-quality study • Several studies with some limitations

Code	Quality of Evidence	Definition
C	Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. • One or more studies with severe limitations
D	Very Low	Any estimate of effect is very uncertain. • Expert opinion • No direct research evidence • One or more studies with very severe limitations

GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group 2011 (modified by the EBM Guidelines Editorial Team).

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Deep venous thrombosis

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Intended Users

Health Care Providers

Physicians

Guideline Objective(s)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

Target Population

Patients with deep vein thrombosis and those at risk for thromboembolism

Interventions and Practices Considered

Evaluation/Risk Assessment/Diagnosis

1. Risk factor assessment
2. Clinical assessment of signs and symptoms (e.g., pain, oedema, Homan's sign, dilation of superficial veins)
3. Differential diagnosis
4. Scoring pretest probability of deep venous thrombosis (DVT)
5. D-dimer testing
6. Ultrasonography
7. Venography, if indicated
8. Other laboratory tests (e.g., thrombophilia screening)

Treatment/Management/Prevention

1. Choosing site of treatment (hospital versus home)
2. Anticoagulant therapy
    - Low-molecular-weight heparin (LMWH), dalteparin, enoxaparin
    - Warfarin
    - Fondaparinux
3. Thrombolytic therapy
4. Surgery
5. Other treatment (e.g., elastic bandaging/graduated compression stockings)
6. Patient education

Major Outcomes Considered

- Sensitivity and specificity of diagnostic assessments
- Treatment effect on:
    - Incidence of pulmonary embolism
    - Frequency of post-thrombotic changes
    - Recurrence of venous thromboembolism
- Adverse effects

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The evidence reviewed was collected from the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

Comprehensive and systematic searches were conducted for all topics for which the Finnish Medical Society Duodecim produce national guidelines. As most of the evidence summaries were based on systematic reviews (of which Cochrane reviews were the most important), the search dates are available in the original reviews.

Specific Search Strategy

The update of this guideline includes several systematic reviews with a current care search date of November 12, 2007.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of the Quality of Evidence

Code	Quality of Evidence	Definition
A	High	Further research is very unlikely to change confidence in the estimate of effect. • Several high-quality studies with consistent results • In special cases: one large, high-quality multi-centre trial
B	Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate. • One high-quality study • Several studies with some limitations
C	Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. • One or more studies with severe limitations
D	Very Low	Any estimate of effect is very uncertain. • Expert opinion • No direct research evidence • One or more studies with very severe limitations

GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group 2011 (modified by the EBM Guidelines Editorial Team).

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Not stated

Evidence Supporting the Recommendations

References Supporting the Recommendations

Anand SS, Wells PS, Hunt D, Brill-Edwards P, Cook D, Ginsberg JS. Does this patient have deep vein thrombosis. JAMA. 1998 Apr 8;279(14):1094-9. PubMed

Bernardi E, Camporese G, Buller HR, Siragusa S, Imberti D, Berchio A, Ghirarduzzi A, Verlato F, Anastasio R, Prati C, Piccioli A, Pesavento R, Bova C, Maltempi P, Zanatta N, Cogo A, Cappelli R, Bucherini E, Cuppini S, Noventa F, Prandoni P, Erasmus Study Group. Serial 2-point ultrasonography plus D-dimer vs whole-leg color-coded Doppler ultrasonography for diagnosing suspected symptomatic deep vein thrombosis: a randomized controlled trial. JAMA. 2008 Oct 8;300(14):1653-9. PubMed

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Watson LI, Armon MP. Thrombolysis for acute deep vein thrombosis. Cochrane Database Syst Rev. 2004;(4):CD002783. [34 references] PubMed

Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, Clement C, Robinson KS, Lewandowski B. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. Lancet. 1997 Dec 20-27;350(9094):1795-8. PubMed

Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis. JAMA. 2006 Jan 11;295(2):199-207. [40 references] PubMed

Type of Evidence Supporting the Recommendations

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate diagnosis, prevention and treatment of deep venous thrombosis and identification of patient groups at risk
- Prevention of pulmonary embolism and post-thrombotic syndrome in patients at risk

Potential Harms

- Possible complications of anticoagulant and thrombolytic therapy include bleeding and emboli.
- The radiation exposure is minimal in venography and, for example, pregnancy is not a contraindication to the investigation. However, an obstetrician should be consulted before the investigation is carried out.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Finnish Medical Society Duodecim. Deep vein thrombosis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2011 Nov 21 [Various].

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2001 Apr 30 (revised 2011 Nov 21)

Guideline Developer(s)

Finnish Medical Society Duodecim - Professional Association

Source(s) of Funding

Finnish Medical Society Duodecim

Guideline Committee

Editorial Team of EBM Guidelines

Composition of Group That Authored the Guideline

Primary Author: Veli-Pekka Harjola

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Deep vein thrombosis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2010 Aug 3 [Various].

Guideline Availability

This guideline is included in "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on August 28, 2001. The information was verified by the guideline developer as of October 26, 2001. This summary was updated by ECRI on December 9, 2002, July 1, 2004, February 24, 2005, and May 25, 2006. This summary was updated by ECRI on March 6, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin sodium). This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on September 7, 2007 following the revised U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin). This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection. This summary was updated by ECRI Institute on December 26, 2008 following the FDA advisory on Innohep (tinzaparin). This summary was updated by ECRI Institute on July 27, 2010 following the FDA drug safety communication on Heparin. This NGC summary was updated by ECRI Institute on March 26, 2012. This summary was updated by ECRI Institute on March 10, 2014 following the U.S. Food and Drug Administration advisory on Low Molecular Weight Heparins.

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